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EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,620	GRAFF ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *1-3, 6-8, 14, 56 and 58 in part as they apply to protein based methods and claims 13, 15-55, 57, 59, and 60 in their entirety* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6-8, 14, 56 and 58 in part as they apply to nucleic acid based methods, and claims 4, 5, 9-12 in their entirety* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/31/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Election filed September 14, 2006 in response to the Office Action of August 9, 2006 is acknowledged and has been entered.

2. Claims 48-50 and 53 were amended by Applicant.

3 New claims 56-60 were added by Applicant.

4. Applicant's election with traverse of Group I, Claims 1-3, 6-8, and 14 in part as they apply to nucleic acid based methods, and claims 4, 5, and 9-13, in their entirety, drawn to nucleic acid based methods for diagnosing breast cancer in a subject and the species (A) FLJ20174, (B) breast cancer, (C) cDNA, and (D) amplifying the nucleic acid, and further electing the nucleic acid SEQ ID NO: 3 is acknowledged.

Applicant's do not traverse the species election between the marker CXCL9 and FLJ20174 and between the cancers breast and ovarian.

5. Applicants' Traversals:

A. Applicants have amended claims 48 and 49 to depend on claim 47 and argue that claim 48 and claim 49 should be rejoined to the appropriate Group. This argument is found persuasive and claim 48 will be rejoined to Group XI and claim 49 will be rejoined to Group X.

B. Claim 50 has been amended to recite only therapeutic agents that bind to gene products. Applicants argue that claim 50 should be assigned in its entirety to Group X. This argument has been considered, but not found persuasive because gene product can read on mRNA as well as protein.

Claim 57 has been added and applicants argue that it should be assigned in its entirety to Group XI because it only recites therapeutic agents that bind to nucleic acids.

This argument is found persuasive and claim 57 will be joined to Group XI as necessary.

C. Applicant argues that claim 47, along with its dependent claims, claims 48 and 49, is improperly joined with claim 50 in Groups X and XI and should be joined with claims 41-43 of Group VII as process and apparatus for its practice. Applicant argues that claims 47-49 should grouped with claim 50 and its dependent claims.

This argument has been considered, but not found persuasive for the reasons of record, and for the following reasons:

Inventions of Group VII and Group X and XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the agents that bind protein gene products of Group X could be used in affinity chromatography and the agent that bind nucleic acids of Group XI could be used to detect the genomic DNA of the gene in a Southern analysis.

D. Applicant argues that the requirement to fragment claims under 35 USC 121 is improper as it violates Applicants' basic right to claim the invention as they choose. Applicants argue that it is improper to require Applicants under 35 USC 121 to divide claims in to "nucleic acid based" and "protein-based" claims. Applicants argues that under In re Weber, 580 F.2d

455, 458, 198 USPQ 328, 332 (CCPA 1978) and In re Haas, 580 F.2d 461,464, 198 USPQ 334, 336 (CCPA 1978), it is never proper for an examiner to reject a Markush claim under 35 U.S.C. § 121. Applicant argues that Section 121 simply does not authorize such a rejection. Id. In re Watkinson, 14 USPQ2d 1407, 1409 (Fed. Cir. 1990). Applicant further argues that it is improper to require applicant under 35 USC 121 to submit related nucleic acid or related protein sequences in separate claims. Applicant argues that the claims to related sequences are Markush claims and it is never proper for an examiner to reject a Markush claim under 35 USC 121.

Applicant's argument has been considered but has not been found persuasive. It is noted that claims are definitions of inventions and the scope of a claim may be limited to a single disclosed embodiment and thus it is proper to restrict within a claim, see MPEP 806.04 (e). Furthermore the restriction between nucleic acid and protein claims and between related nucleic acids and proteins is proper because, although the claims are presented in Markush format, the claims are drawn to multiple products and methods using multiple products which do not share, as a whole, a substantial structural feature disclosed as being essential to their utility. Thus, the analysis of the claims, for restriction purposes, is subject to the findings of the court wherein the court found that unity of invention exists where entities included within a Markush group share a substantial structural feature disclosed as being essential to utility of the invention, In re Harnisch, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Since the members of the group do not share a substantial structural feature disclosed as being essential to utility of the invention, the group as claimed fails the Harnisch test and the claims are not accorded Markush restriction practice because they do not meet the requirements to be accorded Markush practice under MPEP 803.02.

Applicant argues that it is unclear whether the election of nucleic acids and polypeptides for Groups III and VI respectively is for an election of a species or of a Group.

This argument has been considered and found persuasive. Examiner notes that the election statements under Groups III and VI are typographical errors and the elections for nucleic acids and polypeptides should be a Group election, not a species election, as stated for all of the other Groups.

E. Applicant argues that the newly added claim 56 links the methods of Groups I-IV and the subject matter of claim 56 and 58-60 overlap the subject matter of claims 1, 18, and 34.

The argument has been considered, but has not been found persuasive because, although newly added claim 56 links the nucleic acid based inventions properly restricted in the paper mailed august 9, 2006, only claim 56 and claim 58 will be rejoined to Group 1 at this time as they are drawn to the elected invention. The inventions of claims 59-60 are distinct for the reasons of record and although the subject matter might overlap, the search required for these inventions is not coextensive and therefore represents a high level of burden for examiner.

Claim 56 links inventions drawn to diagnosis, prognosis and monitoring of cancer. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 56. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or

divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP 804.01.

F. Applicant argues that the methods of Groups I-VI and new claim 56 are linked as process and apparatus for its practice with Groups VIII and IX and claims 44, 48, and 49.

This argument has been considered, but not been found persuasive for the reasons of record.

G. Applicant argues that the withdrawal of the traversed restriction requirement will not invoke a burdensome search.

This argument has been considered, but not been found persuasive for the reasons of record.

H-1. Applicants argue that the election of species of nucleic acids (mRNA, hnRNA, or cDNA) should be withdrawn because similar databases will be searched and searching these species would not be unduly burdensome.

This argument is found persuasive.

H-2. Applicants argue that the election of a species of nucleic acid detection should be withdrawn because the search is essentially identical and the methods permit the detection of sequences that have a limited degree of dissimilarity from a designated sequence.

The argument has been considered, but has not been found persuasive because the methods are materially distinct methods which differ at least in method steps, reagents and/or dosages and/or schedules used, response variables, and criteria for success and different searches and issues are involved in the examination of each group.

H-3. Applicants argue that the requirement to elect a "species" of assessing the expression pattern of a nucleic acid is improper because the alleged "species" do not belong to a single genus. Applicant argues that Species (1) is a further limitation of steps (a) and/or (b) of claim 34. Applicant argues that species (2) is a further limitation of step (c) of claim 34. Applicant argues that the claimed species do not fall within the same genus.

This argument has been considered, but not found persuasive, because although the species are further limitations of claim 34, assessing the expression pattern of a nucleic acid is generic to the listed species in the Office Action of August 9, 2006 for the reasons of record and fall within the same genus of assessing the expression pattern of a nucleic acid.

H-4. Applicants argue that the requirement to elect a "species" of assessing the expression pattern of a nucleic acid is improper because the alleged "species" do not belong to a single genus. Applicant argues that Species (1) and (3) are further limitations of steps (a) and/or (b) of claim 34. Applicant argues that species (2) is a further limitation of step (c) of claim 34. Applicant argues that the claimed species do not fall within the same genus.

This argument has been considered, but not found persuasive, because although the species are further limitations of claim 34, assessing the expression pattern of a protein is generic

to the listed species in the Office Action of August 9, 2006 for the reasons of record and fall within the same genus of assessing the expression pattern of a nucleic acid.

Although applicant has added a claim that links three previously restricted inventions, the issues remain the same, thus for the reasons set forth previously and above, the restriction requirement is deemed to be proper and is therefore made FINAL.

6. Upon review and reconsideration SEQ ID NO: 4 will be rejoined for examination.

7. Claims 1-60 are pending.

8. Claims 1-3, 6-8, 14, 56 and 58 in part as they apply to protein based methods and claims 13, 15-55, 57, 59, and 60 in their entirety, all SEQ ID NOs, except SEQ ID NO: 3 and 4, have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

9. Claims 1-3, 6-8, 14, 56 and 58 in part as they apply to nucleic acid based methods, and claims 4, 5, 9-12 in their entirety, drawn to nucleic acid based methods for diagnosing breast cancer in a subject and SEQ ID NO: 3 and 4 and the species (A) FLJ20174, (B) breast cancer (C) amplifying the nucleic acid are currently under consideration.

Specification

10. The disclosure is objected to because of the following informalities: The number is missing after SEQ ID NO: in paragraph 0034.

Appropriate correction is required.

Claim Objections

11. Claim 5 is objected to because of the following informalities: The phrase "is an up-regulated of at least" is grammatically incorrect. Appropriate correction is required.

12. Claim 7 is objected to because of the following informalities: There is no space between 6 and wherein. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-12,14, and 58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1-12, 14, and 58, the phrase "a difference in" renders the claim indefinite because it is unclear what the level of difference is that is necessary for diagnosing breast cancer. Is the required difference for diagnosis of breast cancer 2-fold, 4-fold, 10-fold, or more or less? The degree of difference necessary to practice the claimed invention cannot be determined from the construction of the claims. Thus, the metes and bounds of the claims cannot be determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-12, 14, 56, and 58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method of diagnosing breast cancer in a subject, the method comprising comparing the expression pattern of FLJ20174 nucleic acid in a sample from a subject with the expression pattern of FLJ20174 nucleic acid in one or more samples from one or more non-cancerous tissues, wherein a difference in the expression pattern of FLJ20174 in the samples is indicative of breast cancer in the subject.

The specification teaches that the present invention provides a method of diagnosing breast cancer in a subject, the method comprising comparing the expression pattern of FLJ20174 in a sample from a subject with the expression pattern of FLJ20174 in samples from one or more non-cancerous tissues.

The specification teaches that using RT-PCR that FLJ20174 is expressed in several normal human tissues (n=18), however the level of expression is generally lower than that detected in breast cancers (n=4), see Example 2 and Figs. 4 and 5. The specification teaches that importantly, the "splice variant" isoform of FLJ20174 appeared to be expressed at higher levels in the breast cancers compared to other normal human tissues whereas the "wild type" isoform was detected at similar levels, see Example 2 and Fig. 6. The specification teaches that this may indicate that the "splice variant" isoform is a more cancer-specific target. The specification teaches that, using RT-PCR, FLJ20174 was overexpressed in 75% of the ductal breast

carcinomas (n=12) examined compared to normal breast tissue (n=12), see Example 2 and FIG. 7. The specification teaches that the "wild type" and "splice variant" isoforms displayed identical patterns of expression in the breast cancers, see Example 2 and Fig. 8.

The specification teaches that, using RT-PCR, FLJ20174 was also found to be overexpressed in approximately 58% of the ovarian cancers examined (n=12) relative to normal ovary tissue (n=9), see Example 2 and Fig. 9. The specification teaches that similar to that observed in breast cancer, the "wild type" and "splice variant" isoforms exhibited similar patterns of expression in the ovarian cancers, see Example 2 and Fig. 9.

The specification teaches, using quantitative RT-PCR that amplified both forms of FLJ20174, that the average level of FLJ20174 in breast cancer was about 5.5-fold higher than the average level in normal breast tissues, see Example 3 and Fig 12. The specification teaches, using quantitative RT-PCR that amplified both forms of FLJ20174, that comparing the average expression level of FLJ20174 in a variety of non-breast normal human tissues (e.g. liver, lung, heart, etc.) to the average expression level in breast cancer tissues, a approximately 8.1-fold increase in expression was observed in breast cancer cells over that of normal non-breast tissues, see Example 3 and Fig 12.

The specification teaches, using quantitative RT-PCR that amplified both forms of FLJ20174, that compared to normal ovarian tissues, the average FLJ20174 level detected in ovarian adenocarcinoma was approximately 6.6-fold higher, see Example 3 and Fig 12. However, the specification teaches, that the average FLJ20174 expression levels in non-ovarian normal human tissues was approximately equivalent to the expression level found in ovarian adenocarcinomas, see Example 3 and Fig 12.

Examiner notes that it is assumed for examination purposes that SEQ ID NO: 3 is the wild type FLJ20174 and SEQ ID NO: 4 is the splice variant given that the splice variant is missing an exon (thus it would be shorter in length) and the Sequence Listing teaches that SEQ ID NO: 3 is 4669 nucleotides in length and SEQ ID NO: 4 is 4595 nucleotides in length.

Given the lack of clarity in the specification as to whether the wild type form of FLJ20174, the splice variant form of FLJ20174, or both forms are overexpressed in breast and ovarian cancer, it is assumed for examination purposes that both isoforms of FLJ20174 are increased in breast and ovarian cancers, not just one isoform.

One cannot extrapolate the teachings of the specification to the enablement of the claims because it is clear from the teachings of the specification that FLJ20174 RNA increases in ovarian cancer as well as breast cancer as taught in the specification, see Example 3 and Fig 12. Thus, based on comparing the FLJ20174 nucleic acid expression pattern alone in a sample from a subject with the FLJ20174 nucleic acid expression in one or more samples from one or more non-cancerous tissues, even if it were to be found that there was differential expression of FLJ20174 nucleic acid compared to normal control, one could not predictably distinguish between breast cancer and another cancer, such as ovarian cancer, to diagnose breast cancer because it appears that both present with the same marker.

In particular, Boyd (The Basic Science of Oncology, 1992, McGraw-Hill, Inc., p.379) teaches that diagnostic tests are used to distinguish patients with and without a particular disease, see p.379, right column. Given that FLJ20174 RNA is overexpressed in both ovarian cancers and breast cancer it is not clear from the teachings of the specification how one would diagnose breast cancer by determination of the FLJ20174 RNA expression pattern alone when FLJ20174

RNA overexpression is not solely specific for breast cancer. Thus, undue experimentation would be required to demonstrate that the FLJ20174 RNA expression pattern is solely diagnostic for breast cancer and not for other cancers by, for example, determining the FLJ20174 RNA expression pattern in a larger set of ovarian tumors or by determining the FLJ20174 RNA expression pattern in multiple other tumor types.

Applicant is reminded that MPEP 2164.03 teaches "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 428 F.2d 833, 166 USPQ 18, 24 (CCPA 1970) the amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly state in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order for it to be enabling. Given only lack of guidance in the specification, no one skilled in the art would accept the assertion that the claimed invention would function as contemplated or as claimed based only on the information in the specification and that known in the art at the time the invention was made.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention will

function as contemplated with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

15. If applicant were able to overcome the rejection set forth above, Claims 1-12, 14, 56, and 58 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing breast cancer in a subject, the method comprising comparing the expression pattern of FLJ20174 nucleic acid in a sample from a subject with the expression pattern of FLJ20174 nucleic acid in one or more samples from one or more non-cancerous tissues, wherein a difference in the expression pattern of FLJ20174 nucleic acids in the samples is indicative of breast in the subject, wherein FLJ20174 consists of SEQ ID NO: 3 or SEQ ID NO: 4, does not reasonably provide enablement for a method of diagnosing breast cancer in a subject, the method comprising comparing the expression pattern of FLJ20174 nucleic acids nucleic acid in a sample from a subject with the expression pattern of FLJ20174 nucleic acid in one or more samples from one or more non-cancerous tissues, wherein a difference in the expression pattern of FLJ20174 in the samples is indicative of breast cancer in the subject or by detecting the presence in the sample of a nucleic acid comprising 30 or more contiguous nucleotides of SEQ ID NO: 3 or SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method of diagnosing breast cancer in a subject, the method comprising comparing the expression pattern of FLJ20174 nucleic acid in a sample from a subject with the expression pattern of FLJ20174 nucleic acid in one or more samples from one

or more non-cancerous tissues or by detecting the presence in the sample of a nucleic acid comprising 30 or more contiguous nucleotides of SEQ ID NO: 3 or SEQ ID NO: 4, wherein a difference in the expression pattern of FLJ20174 in the samples is indicative of breast cancer in the subject.

This means that one can diagnose breast cancer by detecting a difference in the expression pattern of **any FLJ20174** nucleic acid or by detecting a difference in the expression pattern of **any** nucleic acid comprising 30 or more contiguous nucleotides of SEQ ID NO: 3 or SEQ ID NO: 4.

The specification teaches that a variety of methods can be employed to screen for the presence of, or detect and/or assay levels of, FLJ20174 nucleic acid sequences in a biological sample as compared to normal controls, see para. 0050.

The specification teaches that the term "FLJ20174 nucleic acid sequence" and the like refers to the nucleic acid sequence disclosed as SEQ ID NO: 3 and SEQ ID NO: 4 and homologs, mutations or variants of those sequences found in a subject, see para. 0035. Thus, it is noted that, given the definition of the term FLJ20174, that it is assumed for examination purposes that the term means any homolog, variant of SEQ ID NO: 3 and 4.

One cannot extrapolate the teaching of the specification to the enablement of the claims because the specification does not provide teachings or working examples which would provide sufficient guidance to allow one of skill in the art to use the methods as claimed because they encompass detecting a whole universe of universe of undefined FLJ20174 nucleic acid molecules whose association with breast cancer cannot be predicted. Additionally, the detection of a nucleic acid that comprises 30 or more contiguous nucleotides of SEQ ID NO: 3 or 4

encompasses nucleic acids molecules that are less than 1% identical to SEQ ID NO: 3 or 4 given that SEQ ID NO: 3 is 4669 nucleotides in length and SEQ ID NO: 4 is 4595 nucleotides in length. Thus, the claims read on detection of polynucleotides that range from those that lack significant complementarity to those that are completely complementary to SEQ ID NO: 3 or 4 or in fact to any homolog or variant thereof given that comprises 30 contiguous resides of SEQ ID NO: 3 or 4. Clearly, it would be expected by one of ordinary skill in the art that a substantial number of the of the FLJ20174 nucleic acids and nucleic acids comprising 30 contiguous nucleotides of SEQ ID NO: 3 or 4 **would not** be diagnostically associated with breast cancer and it would not be expected that any of the polynucleotides without, substantial complementarity to the polynucleotide SEQ ID NO: 3 OR 4, could function as claimed.

The specification does not provide guidance or exemplification on how to use the multitude of nucleic acids encompassed by the claims for the diagnosis of breast cancer. The relationship of these numerous nucleic acid molecules to breast cancer is unknown and unpredictable. In view of the above, one of skill in the art would be forced into undue experimentation in order to practice the invention as claimed.

16. If applicant were able to overcome the rejection set forth above, 1-12, 14, 56, and 58 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing breast cancer in a subject, the method comprising comparing the expression pattern of FLJ20174nucleic acid in a sample from a subject with the expression pattern of FLJ20174 nucleic acid in one or more samples from one or more non-cancerous tissues, wherein **increased expression** of FLJ20174nucleic acid in the samples is

indicative of breast cancer in the subject, does not reasonably provide enablement for a method of diagnosing breast cancer in a subject, the method comprising comparing the expression pattern of FLJ20174 nucleic acid in a sample from a subject with the expression pattern of FLJ20174 nucleic acid in one or more samples from one or more non-cancerous tissues, wherein a difference in the expression pattern of FLJ20174 nucleic acid in the samples is indicative of breast cancer in the subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a method of diagnosing breast cancer in a subject, the method comprising comparing the expression pattern of FLJ20174 nucleic acid in a sample from a subject with the expression pattern of FLJ20174 nucleic acid in one or more samples from one or more non-cancerous tissues, wherein a difference in the expression pattern of FLJ20174/ SEQ ID NO: 3 in the samples is indicative of breast cancer in the subject.

This means that one can diagnose breast cancer by determining if the FLJ20174 nucleic acid expression is increased or **decreased** in breast tissue suspected of being cancerous and any other normal tissue type.

The specification teaches that the present invention provides a method of diagnosing breast cancer in a subject, the method comprising comparing the expression pattern of FLJ20174 in a sample from a subject with the expression pattern of FLJ20174 in samples from one or more non-cancerous tissues, see para. 0010.

The specification teaches that using RT-PCR that FLJ20174 is expressed in several normal human tissues (n=18), however the level of expression is generally lower than that

detected in breast cancers (n=4), see Example 2 and Figs. 4 and 5. The specification teaches that importantly, the "splice variant" isoform of FLJ20174 appeared to be expressed at higher levels in the breast cancers compared to other normal human tissues whereas the "wild type" isoform was detected at similar levels, see Example 2 and Fig. 6. The specification teaches that this may indicate that the "splice variant" isoform is a more cancer-specific target. The specification teaches that, using RT-PCR, FLJ20174 was overexpressed in 75% of the ductal breast carcinomas (n=12) examined compared to normal breast tissue (n=12), see Example 2 and FIG. 7. The specification teaches that the "wild type" and "splice variant" isoforms displayed identical patterns of expression in the breast cancers, see Example 2 and Fig. 8.

The specification teaches that using quantitative RT-PCR that amplified both forms of FLJ20174 that the average level of FLJ20174 in breast cancer was about 5.5-fold higher than the average level in normal breast tissues, see example 3 and Fig 12. The specification teaches, using quantitative RT-PCR that amplified both forms of FLJ20174, that comparing the average expression level of FLJ20174 in a variety of non-breast normal human tissues (e.g. liver, lung, heart, etc.) to the average expression level in breast cancer tissues, a approximately 8.1-fold increase in expression was observed in breast cancer cells over that of normal non-breast tissues see Example 3 and Fig 12.

One cannot extrapolate the teachings of the specification to the scope of the claims because only an increase in the expression of FLJ20174 RNA appears to be associated with breast cancer and given the teaching of the specification no one would think it more likely than not that breast cancer could be diagnosed by a reduction in FLJ20174 RNA compared to normal control.

The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention as currently claimed would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

17. Claims 1-12, 14, 56, and 58 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 1-12, 14, 56, and 58 are broadly drawn to a method of diagnosing breast cancer in a subject, the method comprising comparing the expression pattern of FLJ20174 nucleic acid in a sample from a subject with the expression pattern of FLJ20174 nucleic acid in one or more samples from one or more non-cancerous tissues, wherein a difference in the expression pattern of FLJ20174 in the samples is indicative of breast cancer in the subject. As it is drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of FLJ20174 nucleic acids whose difference in expression diagnoses breast cancer per Lilly by structurally describing a representative number of FLJ20174 nucleic acids whose difference in expression diagnoses breast cancer or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the FLJ20174 nucleic acids whose difference in expression diagnoses breast cancer required to practice the method of claim 1 in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any FLJ20174 nucleic acids whose difference in expression diagnoses breast cancer, nor does the specification provide any partial structure of such nucleic acid, nor any physical or chemical characteristics of the FLJ20174 nucleic acids whose difference in expression diagnoses breast cancer, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a SEQ ID NO: 3 and SEQ ID NO: 4, this does not provide a description of the FLJ20174 nucleic acids

whose difference in expression diagnoses breast cancer that would satisfy the standard set out in Enzo.

The specification also fails to describe the FLJ20174 nucleic acids whose difference in expression diagnoses breast cancer by the test set out in Lilly. The specification describes only a SEQ ID NO: 3 and SEQ ID NO: 4. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the FLJ20174 nucleic acids whose difference in expression diagnoses breast cancer that is required to practice the claimed invention. Since the specification fails to adequately describe the FLJ20174 nucleic acid which is to be detected, it also fails to adequately describe the method for diagnosing breast cancer.

18. Claims 9-12 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 9-12 are drawn to the method of claim 1, wherein the expression pattern of FLJ20174 is determined by detecting the presence in the sample of a nucleic acid comprising 30 or more contiguous nucleotides SEQ ID NO: 3 or SEQ ID NO: 4. As it is drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d

1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial

structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of a nucleic acid comprising 30 or more contiguous nucleotides SEQ ID NO: 3 or SEQ ID NO: 4 that is useful for diagnosing breast cancer, per Lilly by structurally describing a representative number of nucleic acids comprising 30 or more contiguous nucleotides SEQ ID NO: 3 or SEQ ID NO: 4 or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe a nucleic acid comprising 30 or more contiguous nucleotides SEQ ID NO: 3 or SEQ ID NO: 4 that is useful for diagnosing breast cancer required to practice the method of claim 1 in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any nucleic acid comprising 30 or more contiguous nucleotides SEQ ID NO: 3 or SEQ ID NO: 4 that is useful

for diagnosing breast cancer, nor does the specification provide any partial structure of such nucleic acid, nor any physical or chemical characteristics of a nucleic acid comprising 30 or more contiguous nucleotides SEQ ID NO: 3 or SEQ ID NO: 4 that is useful for diagnosing breast cancer, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses SEQ ID NO: 3and SEQ ID NO: 4, this does not provide a description of a nucleic acid comprising 30 or more contiguous nucleotides SEQ ID NO: 3 or SEQ ID NO: 4 that is useful for diagnosing breast cancer that would satisfy the standard set out in Enzo.

The specification also fails to describe a nucleic acid comprising 30 or more contiguous nucleotides SEQ ID NO: 3 or SEQ ID NO: 4 that is useful for diagnosing breast cancer by the test set out in Lilly. The specification describes only SEQ ID NO: 3 and SEQ ID NO: 4. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of a nucleic acid comprising 30 or more contiguous nucleotides SEQ ID NO: 3 or SEQ ID NO: 4 that is useful for diagnosing breast cancer to practice the claimed invention. Since the specification fails to adequately describe a nucleic acid comprising 30 or more contiguous nucleotides SEQ ID NO: 3 or SEQ ID NO: 4 that is useful for diagnosing breast cancer to be detected, it also fails to adequately describe the method for diagnosing breast cancer.

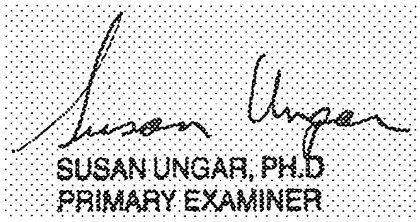
19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642



PJR